

**Remarks/Arguments**

Claims 1-28 have been canceled.

New claims 29-52 have been added. New claims 29-44 correspond in part to old claims 1-17. Claims 45 and 46 correspond in part to old claims 20 and 21. Claims 47, 48, 49 and 50 substantially correspond to old claims 22, 26, 27 and 28. New claims 51 and 52 are presented for the first time.

Claims 29-52 are pending.

**Rejection under 35 USC §102**

The Examiner has finally rejected claims 1, 2, 4-10, 12-14, 16-18, 20-21, and 23-24 over WO 97/00248. Applicants believe that recitation WO 97/00248 in the outstanding office action was a typing error (transposing of the publication number with the international application number) and that the Examiner in fact meant to cite WO 97/39747. Thus, Applicants remarks herein are addressed to the Examiner's rejections over WO 97/39747.

New independent claims 29 and 51 require that a dew point of the drying gas be selected such that the spray dried particles formed when a liquid feed is contacted with the drying gas possess certain desired aerodynamic properties that are particularly suitable for inhalation. WO 97/39747 does not teach or suggest every aspect of the new independent claims. WO 97/39747 describes spray drying a paracetamol-containing composition such that the spray dried particles are sufficiently coated for the purpose of taste masking and sustained release. WO 97/39747 does not disclose or suggest spray dried particles having desired aerodynamic properties particularly suitable for inhalation, nor does WO 97/39747 suggest or disclose selecting a dew point of a drying gas to correspond to the formation of spray dried particles having targeted aerodynamic properties particularly suited for inhalation, as is presently claimed. WO 97/39747 instead describes that a drying gas exhibiting a low dew point aids in the formation of a substantially continuous coating on the resulting particles. The additional discussion on pages 10-12 of WO 97/39747 referred to by the Examiner, relates to controlling other

process parameters for the purposes of forming a range of coats on particles and does not disclose or suggest that selecting and controlling specific process parameters relating to moisture content of the drying gas, such as dew point, can result in particles having specific, desired aerodynamic characteristics and that are suitable for inhalation.

Similarly, claims 44, 45, and 47 (which substantially correspond to previous claims 17, 20 and 22), all require that the dew point of the drying gas correspond to one or more targeted aerodynamic characteristics of the particles formed when a liquid feed is contacted with the drying gas. For the reasons discussed above, WO 97/39747 does not disclose or suggest that selecting a dew specific dew point corresponds to specific characteristics of particles formed by contacting a liquid feed with the drying gas.

In addition, Applicants respectfully disagree with the Examiner's assertion that the tap density and the MMAD of the particles described in WO 97/39747 are the same as those described by Applicants because the dew point range of the drying gas in WO 97/39747 is the same as that of Applicants' invention. Using the equation for calculating the aerodynamic diameter on page 16, line 27 of the present application ( $d_{aer} = d_g \sqrt{p_{tap}}$ ), and taking the median geometric diameter ( $d_g$ ) disclosed on page 5 line 10 from WO 97/39747 (100 $\mu$ m) and further assuming for argument purposes only that the tap density of WO 97/39747's particles is the same as that disclosed by Applicant (less than 0.4 g/cm<sup>3</sup>) the equation becomes  $d_{aer} = 100\mu\text{m} \sqrt{0.4}$  and  $d_{aer} = 63 \mu\text{m}$ . Where the tap density is assumed to be 0.1 g/cm<sup>3</sup>, then the  $d_{aer} = 31$  microns. These aerodynamic diameters are clearly too large a particle size for pulmonary delivery. In contrast, Applicants recite that the particles must be suitable for pulmonary delivery and an MMAD or aerodynamic diameter of the particles of the invention is between about 1  $\mu$ m and 3  $\mu$ m. Therefore, the Examiner's assertion that WO 97/39747's MMAD is the same as applicants is incorrect.

Thus, the Examiner's assertion is incorrect and the particles disclosed in WO 97/39747 are not inherently aerodynamically light particles suitable for inhalation as is presently claimed.

Because WO 97/39747 does not teach every aspect of the invention as claimed, WO 97/39747 does not anticipate the invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 25-28 under 35 USC §103 (a)

The Examiner has rejected claims 25-28 as being unpatentable over WO 97/00248. New Claims 43-50 substantially correspond to old claims 26-28. As discussed above, the citation of WO 97/00248 is believed to be in error and that the Examiner in fact meant to cite WO 97/39747. Thus, Applicants remarks herein are addressed to the Examiner's rejections over WO 97/39747.

According to the Examiner, WO 97/39747 teaches spray drying a pharmaceutical composition using a drying gas with a dew point of less than 0 degrees Celsius and also teaches that the drying gas exhibiting a low dew point aids in the production of a substantially continuous coating. Applicant submits that WO 97/39747's discussion of dew point and other process parameters as they relate to optimizing the characteristics of the coating on the particles described therein does not teach, disclose or suggest the method of manipulating process parameters relating to the moisture content of a drying gas (such as dew point and vapor content) such that spray dried particles are produced having targeted aerodynamic properties including targeted tap densities and targeted aerodynamic diameters as is claimed in claims 43-50.

Furthermore, the process controls described in WO 97/39747 are for the purpose of providing a particle coating that is intended to mask taste and provide sustained release as the particles are intended for oral delivery. The present invention solves a completely different problem and instead addresses the formation of particles having targeted aerodynamic properties suitable of inhalation by correlating certain process parameters (dew point, vapor pressure and other measurements of humidity) with specific desired aerodynamic particle characteristics and then using those corresponding process parameters to produce the desired particles. Therefore, one skilled in the art would not be motivated to apply the teachings of a reference that is directed to optimizing the

characteristics of the coating on particles for oral delivery to obtain the Applicants claimed invention.

In addition to the above, the Examiner notes that WO 97/39747 does not teach the vapor pressure of a drying gas. However, the Examiner asserts that in the absence of showing that dew point and vapor pressure are not a function of each other, it is deemed obvious to one of ordinary skill in the art at the time the invention was made that controlling the dew point of the drying gas would also control vapor pressure. Applicant is uncertain of the relevance of this statement. Even if dew point and vapor content or vapor pressure were a function of each other, WO 97/39747 still does not provide any motivation to produce particles having specific aerodynamic properties by adjusting the dewpoint, vapor content or vapor pressure of the drying gas.

Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1, 2, 5-18, 22-23 and 25-28 under 35 USC §103 (a)

The Examiner has rejected claims 1, 2, 5-18, 22-23 and 25-28 under 35 USC §103 (a) as being unpatentable over Edwards et al. (US Pat. No. 5,985,309) in view of WO 01/23821 or vice versa. Applicants respectfully disagree and will address this rejection as it relates to new claims 1-52.

According to the Examiner, Edwards discloses that the composition of the spray dried material and the spray drying parameters affect the aerodynamic properties of particles but that Edwards does not specify additional spray drying parameters, i.e. dew point/vapor pressure of the drying gas. According to the Examiner, it would have been obvious to combine the teachings of Edwards and WO 01/23821 since WO 01/23821 teaches that additional parameters such as dew point affects the final product. Applicants respectfully disagree.

WO 01/23821 does not disclose or suggest that the moisture content of a drying gas corresponds to the aerodynamic properties of the resulting spray dried particles. Instead, WO 01/23821 addresses a completely different problem and that is the importance of maintaining optimal spray drying process parameters for coating tablets. According to WO 01/23821, if one or more parameters changes during processing of a

given batch of coated tablets (including humidity), the quality of the end product will be reduced. The term "product quality" as used in WO 01/23821 does not disclose or suggest anything about aerodynamic properties of particles or the desirability of forming particles with aerodynamic qualities suitable for inhalation as disclosed and claimed in the present invention. As WO 01/23821 makes no mention of aerodynamic properties of particles, WO 01/23821 can not then disclose or suggest that adjustments to the humidity of the drying gas can correspond to obtaining particles having the desired aerodynamic properties as claimed.

Therefore Edwards or WO 01/23821, alone or in combination, do not suggest or disclose that the aerodynamic properties of spray-dried particles can be controlled by manipulating the moisture content of a drying gas as is claimed by Applicants. Thus, the claimed invention is not obvious in view of the cited art. Reconsideration and withdrawal of the rejection is respectfully requested.

### **Conclusions**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

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